MEIOSIS

Edited by

Peter B. Moens

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Meiosis

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Preface

This volume celebrates the coming of age of meiosis research. Although meiosis is the essence of sexual reproduction—and thereby deserves a central position in biological research—rarely has a symposium or a monograph been devoted to this topic. Meiosis usually dwells in the wings at genetic, chromosome, and cell biology meetings, while its rival, the mitotic cell cycle, frequently takes center stage.

Modern meiosis research became more consolidated when, at the conclusion of the 1973 annual meeting of the Genetics Society of America, Herbert Stern invited meiosis-oriented researchers to La Jolla for an informal discussion. There the topic was analyzed not so much within the confines of classical cytogenetics, but more in terms of its biochemistry, its recombinational mechanisms, and its ultrastructural phenomena.

Subsequently, meiosis claimed a more prominent position through "A Discussion on the Meiotic Process," organized by R. Riley, M. D. Bennett, and R. B. Flavell for the Royal Society of London on December 10 and 11, 1975 (*Phil. Trans. R. Soc. Lond. B* **277,** 183–376, 1977). On this occasion, new techniques and insights came to the fore, symbolized to an extent by the frontispiece depicting the ingenious Counce–Meyer spermatocyte surface spread, which revolutionized the study of meiotic chromosome behavior and structure for the next decade and beyond. To my own pleasure, the structural analysis of meiotic processes in yeast (*Saccharaomyces cerevisiae*) has since become commonplace. Curiosity about the genetic regulation of meiosis-specific functions is implicit in most papers, and presently the genetic dissection of meiosis has indeed become a field of intense research. The many observations on the synaptonemal complex—the ubiquitous nuclear organelle of the meiotic prophase nucleus—demanded knowledge of its molecular structure. Through the use of antibodies this information is now emerging.

As ten years have passed since the Royal Society discussion, it was a timely decision to organize a monograph on this topic. I gladly accepted the opportunity to bring together a number of researchers in the field to report on progress and,

thereby, to show the direction of future research. I am pleased to acknowledge the personal assistance of my wife, Maria, and of my colleague Barbara Spyropoulos in the administration of the task. I am particularly grateful to Dr. A. Zimmerman for the initiative, to the staff of Academic Press for their assistance, and to the twelve outstanding scientists who were willing to contribute to this volume. We all share an interest in the topic and hope this volume will instruct the reader in the processes of meiosis and possibly recruit some into its study.

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Meiosis

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1

Introduction to Meiosis

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I. THE BASICS

Chromosome behavior at meiosis differs in detail between species. To avoid unwarranted generalizations, I will illustrate chromosome behavior at meiosis by a specific example, the grasshopper *Chloealtis abdominalis*. To demonstrate the universality of the process of meiosis, the Easter lily *Lilium longiflorum* is shown in comparison. Variations in the regulation of meiosis are illustrated in *Chloealtis conspersa,* a close relative of *C. abdominalis*.

In sexually reproducing organisms, each of two parents contributes one set of chromosomes, a genome, to an offspring. In *C. abdominalis,* one genome consists of nine chromosomes with or without a sex chromosome (X). There are two long chromosomes with the centromere near the middle (Fig. 1j). These two metacentrics look V-shaped. The remainder have the centromere near the end; these telocentrics have a rodlike appearance. Chromosome #3 and the X chromosome are the two larger rods and chromosomes #4 to #9 are successively smaller. Upon fertilization between an egg (one genome + X) and a spermatozoan (one genome), the resulting zygote has two genomes plus an X chromosome per nucleus. The chromosomes of such a nucleus are shown in Fig. 1a, b. There are two of each kind of chromosome, except the X chromosome. The two smallest chromosomes #9 are in the middle of the group and the four V-shaped chromosomes are on the periphery. To emphasize that there are two genomes in Fig. 1b, one set of chromosomes is drawn in solid black and the other is stippled. The positions of the chromosomes relative to each other appear

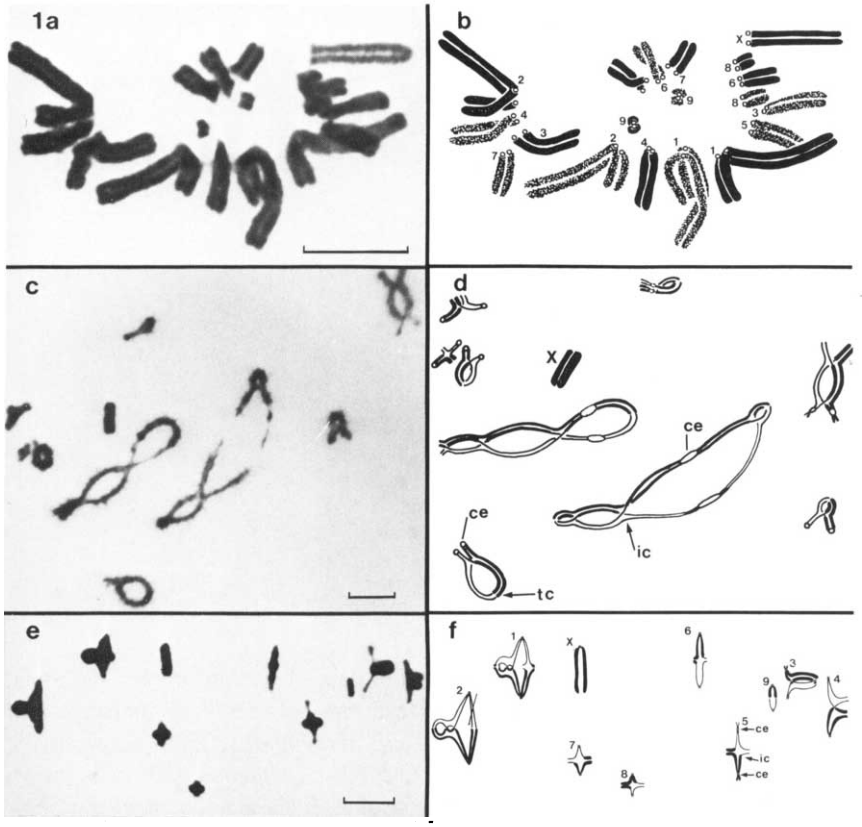
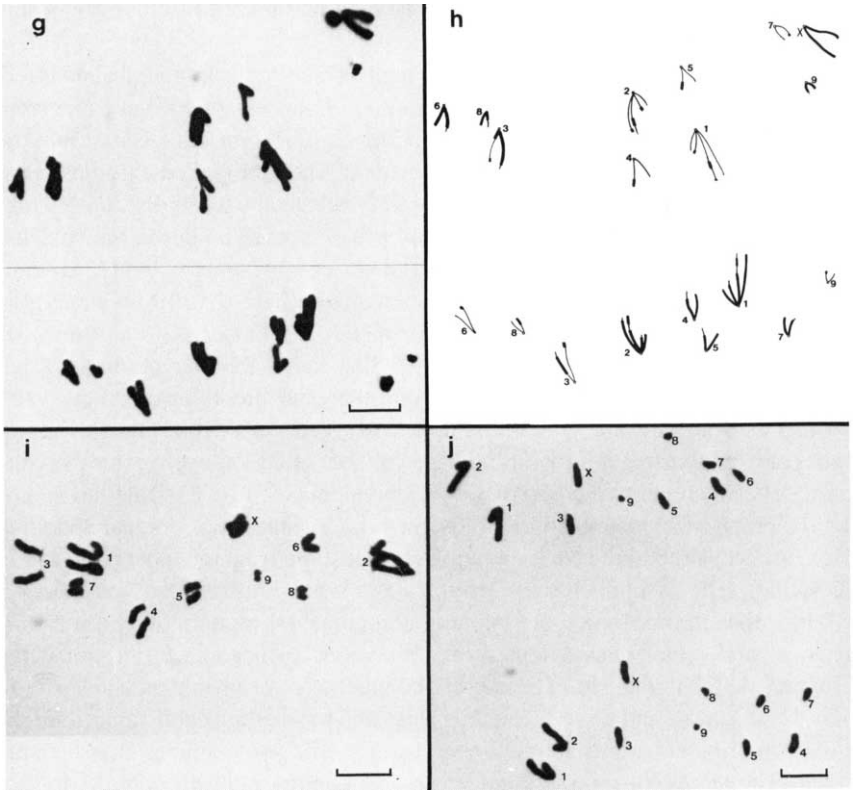


Fig. 1. Meiosis in the male grasshopper *Chloealtis abdominalis*. All scale bars are 10 μm. (a) Mitotic metaphase with 18 autosomes and an X chromosome. (b) Diagram of Fig. 1a to demonstrate that the somatic cells have two sets of chromosomes as a result of fertilization between a male and a female gamete, each carrying a single set of nine chromosomes (9 + X in the oocyte). The chromosomes are numbered according to length with the maternal complement in solid black and the paternal contribution stippled. Assignment of origin is arbitrary. The single genome is illustrated in Fig. 1j. (c) During meiosis, corresponding chromosomes of each of the two genomes become paired. As a result, there are now nine bivalents and an X chromosome per spermatocyte nucleus. At the time of pairing, the bivalents are too long and tangled to recognize singly, but after contraction into the diplotene stage of meiosis, the individual bivalents are evident. (d) Diagram of Fig. 1c to illustrate the pairing arrangement of each maternal chromosome (thick line) with the corresponding paternal homologue (thin line). The homologues have formed non-sister chromatid cross connections at several points. These reciprocal crossovers are visible as an interstitial chiasma (ic) or a terminal chiasma (tc, the size of the exchanged segment is too small to be drawn in). Centromere = ce. (e) Meiotic metaphase I. (f) The diagram of Fig. 1e. The centromeres (ce) of each pair of homologues



are directed to opposite poles. The chromosomes that originally came from the female parent (thick line) and the male parent (thin line) are directed randomly to one pole or another (assignment of origins is arbitrary in the drawing). The sister chromatids of each chromosome are still joined and, as a result, crossovers prevent precocious separation of the chromosomes. (g) Anaphase I of meiosis. The essential feature of meiosis, the reduction of two genomes per nucleus to one genome per nucleus, is accomplished at this time. (h) Diagram of Fig. 1g shows that only one homologue of each pair goes to the upper pole and the other to the lower. As a result, each new nucleus has only one set of chromosomes. The mix of thick and thin lines demonstrates the distribution of maternally and paternally derived chromosome material as a result of random assortment of centromeres and of reciprocal genetic exchange. One nucleus receives the unpaired X chromosome. The exchange points are taken from the chiasma positions in metaphase I (Fig. 1e, f). (i) Metaphase II of meiosis. Since the chromosomes are duplicated during S phase prior to pairing, the anaphase I of Fig. 1g can immediately enter second metaphase. Half the metaphase II nuclei have an X chromosome. (j) Anaphase II, the final step in the formation of a nucleus with one genome. The nine chromosomes are identified by number and can be compared with chromosomes of a somatic nucleus in Fig. 1a, b.

random in nuclei of this organism but they may be ordered in other organisms (Chapter 9).

In the adult male, the spermatogenic cells enter meiosis and the uniquely meiotic pairing of chromosomes takes place. The chromosomes that came from one parent become paired to the corresponding chromosomes that came from the other parent. The phenomenon becomes evident when the paired chromosomes, now bivalents, have contracted far enough to be recognized individually (Fig. 1c, d). It is clear that there are no longer 9 + 9 + 1 = 19 bodies in the nucleus. Instead there are 9 bivalents and an unpaired sex chromosome in the *C. abdominalis* spermatocyte nucleus. The oocyte, not shown here, has 10 bivalents, the two paired X chromosomes being one of them. At meiosis, chromosomes become paired after they have duplicated so that there are four chromatids per bivalent. The chromatids of the same chromosome are referred to as sister chromatids and they are genetically identical. The chromatids of two homologues are non-sister chromatids. There can be small or even extensive differences between the two homologues of a bivalent (see Fig. 8). The diagram of Fig. 1d emphasizes that each chromosome which came from one parent (thick black line) is paired to the corresponding chromosome from the other parent (thin black line). The assignments are arbitrary and serve illustrative purposes only.

While the chromosomes are paired, a regulated program of chromosome breakage and repair causes non-sister chromatids to become cross connected (Chapters 4, 5, 6, and 10). These cross connections are visible as chiasmata in Figs. 1c, d, 2b, d, and 8c, e (Chapter 7). At this point, the genetic contributions of the two original parents are no longer distinct. The two genomes have become mixed. The degree of mixing is under genetic control and differs between species. It is an evolutionary adaptation of the organism which can generate or reduce genetic variability between offspring and it can thereby promote similarity or dissimilarity between parents and offspring (Chapter 2).

The synapsis of homologous chromosomes followed by their segregation to separate nuclei is the essential meiotic mechanism whereby sexually reproducing organisms produce cells with a single genome from cells with two genomes. The process of separation starts at the first metaphase of meiosis when the bivalents orient on the equator of the cell (Fig. 1e,f). The microtubules of the spindle become attached to the centromeres, or kinetochores, and appear to pull the centromeres of a bivalent to opposite poles. However, since sister chromatids still adhere to each other, the crossovers between non-sister chromatids prevent the two chromosomes of a bivalent from separating (Fig. 1f). The X chromosome is an exception and may go to either pole. Under abnormal conditions, where the adhesion between sister chromatids or crossing-over is interfered with, precocious separation results in unorderly distribution of chromosomes.

In a microscope preparation of live spermatocytes, metaphase I stage suddenly ends as the separating chromosomes move simultaneously and rapidly (1

μm/min) to the poles of the cell. This first meiotic anaphase (Fig. 1g, h) is the cardinal moment in the meiocyte when the mixture of two genomes is sorted out into two single genomes. Each genome contains a complete set of chromosomes but the two sets are different in genetic detail. If, for example, the metaphase I bivalents of Fig. 1f divide into the anaphase I of Fig. 1h, then the distribution of thick and thin lines represents the mix of original maternal and paternal contributions in the two separating genomes. No two spermatocytes will have the same mix. The thoroughness of the mix is generated from two sources, the random orientation of bivalents at the metaphase plate in regard to parental origin and the exchange between non-sister chromatids.

Since the chromosomes were duplicated before they paired at meiotic prophase, the anaphase I chromosomes can enter the second metaphase of meiosis immediately, without an intervening duplicating stage (Fig. 1i). Metaphase II is followed by a second meiotic anaphase which reduces the single genomes of duplicated chromosomes to single genomes of single DNA content (Fig. 1j).

The remarkable similarity of the meiotic process, even between biological kingdoms, is evident from a comparison of meiosis in a grasshopper (Fig. 1) with meiosis in the Easter lily, *Lilium longiflorum* (Fig. 2). In the lily two sets of 12 chromosomes pair during meiotic prophase producing the pachytene stage of meiosis with an intractable tangle of long bivalents (Fig. 2a). Much of the biochemistry of meiosis discussed in Chapter 10 was done with these chromosomes. When the 12 bivalents shorten during prophase, they become individually recognizable (Fig. 2b). The diplotene bivalents obviously resemble, in chromatid and chiasma structure, those of the grasshopper in Fig. 1c. Both are in fact similar to most organisms that have genetic recombination at meiosis. At metaphase I, the bivalents orient on the equatorial plate in Fig. 2c and the centromeres are directed to the poles (Fig. 2c, d). At anaphase I (Fig. 2e, f) the undivided chromosomes move to the poles (as in Fig. 1g). The segregating chromosomes, consisting of two chromatids each, are already duplicated and can therefore enter metaphase II right away (Fig. 2g). The four single genomes produced by meiosis are evident in Fig. 2h.

II. COMMITMENT TO MEIOSIS

In complex organisms, meiosis is a genetically programmed step in the life of the organism. Meiosis-specific events may not be recognizable as such because they are embedded in the differentiation of the gonad and the gamete (Chapter 11). In free-living single-celled organisms as well as in relatively simple multicellular organisms, meiosis can occur as a response to environmental conditions. Since the environment can be artificially manipulated, the regulation of meiosis

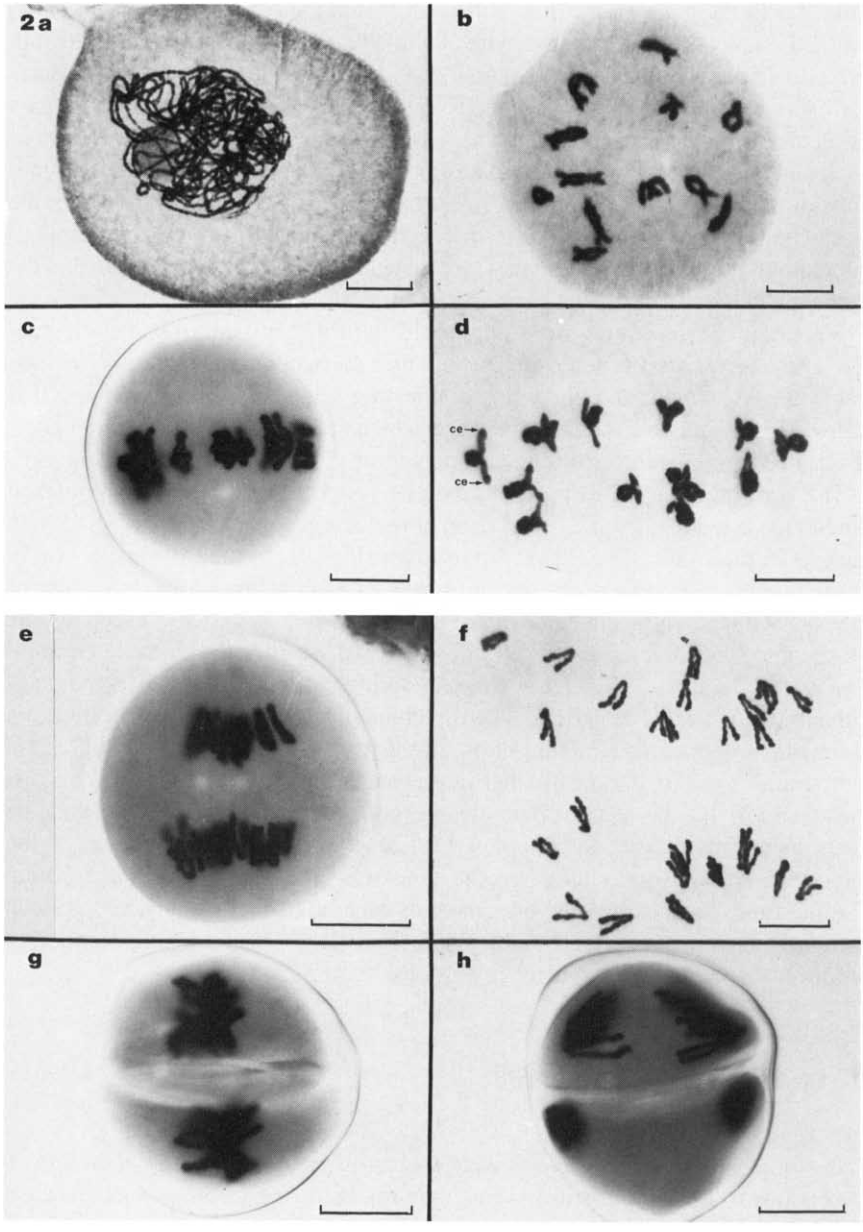


Fig. 2. Meiosis in pollen mother cells of the Easter lily, *Lilium longiflorum*. Bars = 10 μm. (a) During meiotic prophase, after chromosome duplication, the homologous chromosomes synapse and produce 12 long bivalents. This is the ''pachytene'' (thick strand) stage of meiosis. Because of their great lengths, the individual bivalents are not recognizable in this type of preparation. The grey